

AMENDMENTS TO THE CLAIMS

1. **(Original)** A method for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder, said method comprising detecting a marker that is linked to map position 4q35.2 of the human genome in a sample derived from a subject, wherein the detection is indicative of a bipolar affective disorder or a predisposition to a bipolar affective disorder in the subject.

2. **(Original)** The method according to claim 1 wherein the marker linked to map position 4q35.2 is located between or comprises the microsatellite markers selected from the group consisting of:

(i) the microsatellite marker designated D4S1164 (SEQ ID NO: 21) and the microsatellite marker D4S1192 (SEQ ID NO: 27);

(ii) the microsatellite marker designated D4S910 (SEQ ID NO: 22) and the microsatellite marker D4S1374 (SEQ ID NO: 28);

(iii) the microsatellite marker designated D4S3173 (SEQ ID NO: 23) and the microsatellite marker D4S1375 (SEQ ID NO: 29);

(iv) the microsatellite marker designated D4S3236 (SEQ ID NO: 24) and the microsatellite marker designated D4S3051 (SEQ ID NO: 30); and

(v) the microsatellite marker designated D4S2827 (SEQ ID NO: 25) and the microsatellite marker D4S2643 (SEQ ID NO: 31).

3. **(Original)** The method according to claim 1 wherein the marker linked to map position 4q35.2 is located within or comprises the FAT gene.

4. **(Original)** A method for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder, said method comprising detecting a marker within a FAT gene or an expression product thereof that is associated with a bipolar affective disorder in a sample derived from a subject, wherein a presence of the marker is indicative of a bipolar affective disorder or a predisposition to a bipolar affective disorder in the subject.

5. **(Original)** The method according to claim 4 wherein the FAT gene comprises a nucleotide sequence selected from the group consisting of:

(i) a nucleotide sequence at least 80% identical to the nucleotide sequence set forth in SEQ ID NO: 1;

(ii) a nucleotide sequence that encodes a mRNA at least 80% identical to the nucleotide sequence set forth in SEQ ID NO: 2 or 4; and

(iii) a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 3 or 5.

6. **(Original)** The method according to claim 4 wherein the marker is located within the 3' region of the FAT gene.

7. **(Original)** The method according to claim 3 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 139,260 to nucleotide position 170,001 of SEQ ID NO: 1.

8. **(Original)** The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 146,012 to nucleotide position 170,001 of SEQ ID NO: 1.

9. **(Original)** The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 148,108 to nucleotide position 170,001 of SEQ ID NO: 1.

10. **(Original)** The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 148,199 to nucleotide position 170,001 of SEQ ID NO: 1.

11. **(Original)** The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 148,333 to nucleotide position 170,001 of SEQ ID NO: 1.

12. **(Original)** The method according to claim 4 wherein the marker comprises a polymorphism in the FAT gene.

13. **(Original)** The method according to claim 12 wherein the polymorphism is a single nucleotide polymorphism (SNP).

14. **(Original)** The method according to claim 13 wherein the SNP is selected from the group consisting of a cytosine at a position corresponding to nucleotide 80,217 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 130,625 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 130,613 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 139,968 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 139,968 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 142,199 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 142,460 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 145,782 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 146,008 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 146,012 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 146,012 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, a cytosine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 148,199 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 148,333 of SEQ ID NO: 1, a thymine at position 148,333 of SEQ ID NO: 1, a cytosine at a position corresponding to 148,333 of SEQ ID NO: 1, a cytosine at a position corresponding to nucleotide 151,403 of SEQ ID NO: 1 and a thymine at a position corresponding to nucleotide 153,127 of SEQ ID NO: 1.

15. **(Original)** The method according to claim 13 wherein the SNP is selected from the group consisting of a guanine at a position corresponding to nucleotide 139,968 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 146,012 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, a cytosine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 148,333 of SEQ ID NO: 1 and a thymine at position 148,333 of SEQ ID NO: 1.

16. **(Original)** The method according to claim 13 wherein the subject does not have a family history of psychiatric illness and the SNP is selected from the group consisting of a guanine at a position corresponding to 139,968 of SEQ ID NO: 1, a guanine at a position

corresponding to 146,012 of SEQ ID NO: 1, a thymine at a position corresponding to 148,108 of SEQ ID NO: 1 and a thymine at a position corresponding to 148,333 of SEQ ID NO: 1.

17. **(Original)** The method according to claim 13 wherein the subject has a family history of psychiatric illness and the SNP is selected from the group consisting of a thymine at a position corresponding to 139,968 of SEQ ID NO: 1, an adenine at a position corresponding to 146,012 of SEQ ID NO: 1, a cytosine at a position corresponding to 148,108 of SEQ ID NO: 1 and a cytosine at a position corresponding to 148,333 of SEQ ID NO: 1.

18. **(Original)** The method according to claim 4 wherein the marker comprises a nucleic acid comprising a nucleotide sequence at least about 80% identical to at least about 20 contiguous nucleotides in a sequence selected from the group consisting of:

- (i) a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 4;
- (ii) a sequence capable of encoding a polypeptide comprising an amino acid sequence at least 80% homologous to the sequence set forth in SEQ ID NO: 3 and SEQ ID NO: 5; and
- (iii) a sequence complementary to a sequence set forth in (i) or (ii).

19. **(Original)** The method according to claim 4 wherein the marker is detected by hybridising a nucleic acid probe or primer comprising the sequence of the marker to a marker linked to nucleic acid in a biological sample derived from a subject under moderate to high stringency hybridisation conditions and detecting the hybridisation using a detection means, wherein hybridisation of the probe to the sample nucleic acid indicates that the subject being tested is predisposed to or suffers from a bipolar affective disorder.

20. **(Original)** The method according to claim 4 wherein the marker is detected by hybridising a nucleic acid probe or primer comprising the sequence of the marker to a nucleic acid that is linked to the marker in nucleic acid in a biological sample derived from a subject under moderate to high stringency hybridisation conditions and detecting the hybridisation by a detection means, wherein hybridisation of the probe to the sample nucleic acid indicates that the subject being tested is predisposed to or suffers from a bipolar affective disorder.

21. **(Original)** The method according to claim 19 or 20 wherein the detection means is a nucleic acid hybridisation reaction or a nucleic acid amplification reaction.

22. **(Original)** The method according to claim 21 wherein the detection means is a polymerase chain reaction.

23. **(Original)** The method according to claim 19 or 20 wherein the nucleic acid probe or primer comprises a sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57 and SEQ ID NO: 58.

24. **(Original)** The method according to claim 4 wherein the marker is detected by contacting a biological sample derived from the subject with an antibody capable of specifically binding to said marker for a time and under conditions sufficient for an antibody-ligand complex to form and then detecting the complex wherein detection of the complex indicates that the subject being tested is predisposed to or suffers from a bipolar affective disorder.

25. **(Original)** The method according to claim 4 wherein the biological sample comprises a nucleated cell.

26. **(Original)** The method according to claim 25 wherein the biological sample is selected from the group consisting of whole blood, serum, plasma, peripheral blood mononuclear cells (PBMC), a buffy coat fraction, saliva, urine, a buccal cell and a skin cell.

27. **(Original)** The method according to claim 25 wherein the biological sample comprises a cell or cell extract or mixture thereof derived from a tissue selected from the group consisting of a brain, a spinal cord, skin, a lung, a kidney and a pancreas

28. **(Original)** The method according to claim 25 wherein the biological sample comprises a cell or an extract thereof or a mixture thereof isolated using a method selected from the group consisting of amniocentesis, chorionic villus sampling, fetal blood sampling and fetal skin biopsy.

29. **(Currently amended)** The method according to claim 25 ~~any one of claims 25 to 28~~ wherein the biological sample has been derived previously from the subject.

30. **(Original)** A method for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder in a subject, said method comprising:

(i) amplifying nucleic acid from the subject using an amplification reaction, wherein the amplification reaction is performed using a pair of primers selected from the group consisting of:

(a) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 32 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 33;

(b) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 34 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 35;

(c) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 36 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 37;

(d) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 38 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 39;

(e) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 40 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 41;

(f) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 42 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 43;

(g) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 44 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 45;

(h) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 46 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 47;

(i) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 48 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 49;

(j) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 50 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 51;

(k) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 53 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 54; and

(l) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 56 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 57;

(ii) detecting a polymorphism in the amplified nucleic acid from (i), wherein said polymorphism is indicative of a bipolar affective disorder or a predisposition to a bipolar affective disorder in the subject.

31. **(Original)** The method according to claim 30 wherein the polymorphism is detected by determining the nucleotide sequence of the amplified nucleic acid.

32. **(Cancelled)**

33. **(Cancelled)**

34. **(Original)** A probe or primer comprising at least about 20 nucleotides that is capable of selectively hybridizing to the sequence set forth in SEQ ID NO: 1 and detecting a marker in a FAT gene that is associated with a bipolar affective disorder or a predisposition to a bipolar affective disorder.

35. **(Original)** The probe or primer according to claim 34 comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57 and SEQ ID NO: 58.

36. **(Original)** A method for determining a subject that carries a gene or allele of a gene or a polymorphism that is associated with a bipolar affective disorder comprising detecting a marker within a FAT gene that is associated with a bipolar affective disorder in a sample

derived from the subject, wherein detection of said marker indicates that the subject is a carrier of a gene or allele of a gene or a polymorphism is associated with a bipolar affective disorder.

37. **(Currently amended)** A method of treatment or prophylaxis of a bipolar affective disorder comprising:

(i) performing the method of claim 1 ~~any one of claims 1 to 31~~ for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder; and

(ii) administering or recommending a therapeutic for the treatment of bipolar affective disorder.

38. **(Original)** A method for identifying a marker that is associated with a bipolar affective disorder, said method comprising:

(i) identifying a polymorphism or allele within a FAT gene or an expression product thereof;

(ii) analyzing a panel of subjects to determine those that suffer from a bipolar affective disorder, wherein not all members of the panel comprise the polymorphism or allele; and

(iii) determining the variation in the development of a bipolar affective disorder wherein said variation indicates that the polymorphism or allele is associated with a subject's predisposition to a bipolar affective disorder.

39. **(Original)** A method for determining a candidate compound for the treatment of a bipolar affective disorder comprising:

(i) administering a candidate compound to an animal or cell comprising or expressing a marker within a FAT gene that is associated with a bipolar affective disorder and determining the level of FAT expression in said cell or animal;

(ii) administering a candidate compound to an animal or cell that does not comprise or express a marker within a FAT gene that is associated with a bipolar affective disorder and determining the level of FAT expression in said cell or animal; and

(iii) comparing the level of FAT expression at (i) and (ii),

wherein a decreased level of FAT expression at (i) relative to (ii) indicates that the compound is a candidate compound for the treatment of a bipolar affective disorder.

40. **(Original)** A method for determining a candidate compound for the treatment of a bipolar affective disorder comprising:

(i) administering a candidate compound to an animal or cell capable of expressing a FAT gene and determining the level of FAT expression in said cell or animal;

(ii) determining the level of FAT expression in an animal or cell capable of expressing a FAT gene in the absence of the candidate compound; and

(iii) comparing the level of FAT expression at (i) and (ii),

wherein a decreased level of FAT expression at (i) relative to (ii) indicates that the compound is a candidate compound for the treatment of a bipolar affective disorder.

41. **(Original)** The method according to claim 39 or 40 wherein the level of FAT expression is determined by determining the level of FAT mRNA in the cell or animal.

42. **(Currently amended)** A process for identifying or determining a compound or modulator for the treatment of a bipolar affective disorder said method comprising:

(i) performing the method according to either claim 39 or Claim 40 ~~any one of claims 39 to 41~~ to thereby identify or determine a compound for the treatment of a bipolar affective disorder;

(ii) optionally, determining the structure of the compound;

(iii) optionally, providing the name or structure of the compound; and

(iv) providing the compound.

43. **(Currently Amended)** A process of manufacturing a compound for the treatment of a bipolar affective disorder comprising:

(i) determining a candidate compound for the treatment of a bipolar affective disorder by performing the method according to either claim 39 or Claim 40 ~~any one of claims 39 to 41~~; and

(ii) using the compound in the manufacture of a therapeutic or prophylactic for the treatment of bipolar affective disorder.